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Periodontal Manifestations of Chronic Atypical Neutrophilic Dermatositis With Lipodystrophy and Elevated Temperature (CANDLE) Syndrome in an 11 Year Old Patient

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Introduction: Chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE) is an auto inflammatory syndrome caused by an autosomal recessive gene mutation. This very rare syndrome has been reported in only 14 patients worldwide. A number of clinical signs have been reported including joint contractures, muscle atrophy, microcytic anaemia, and panniculitis-induced childhood lipodystrophy. Further symptoms include recurrent fevers, purpuric skin lesions, periorbital erythema and failure to thrive. This is the first reported case of periodontal manifestations associated with CANDLE syndrome.

Case Presentation: An 11 year old boy was referred to Cork University Dental School and Hospital with evidence of severe periodontal destruction. The patient's medical condition was managed in Great Ormond Street Children's Hospital, London. The patient's dental management included initial treatment to remove teeth of hopeless prognosis followed by prosthodontic rehabilitation using removable partial dentures. This was followed by further non-surgical periodontal treatment and maintenance. In the long term, the potential definitive restorative options, including dental implants, will be evaluated in discussion with the patient's medical team.

Conclusion: Periodontitis as a manifestation of systemic disease is one of seven categories of periodontitis as defined by the American Academy of Periodontology 1999 classification system. A number of systemic diseases have been associated with advanced periodontal destruction including Diabetes Mellitus, Leukaemia and Papillon-Lefevre Syndrome. In the case described, treatment necessitated a multidisciplinary approach with input from medical and dental specialities for a young patient with severe periodontal destruction associated with CANDLE syndrome.

KEY WORDS:

Child

Periodontal diseases

Syndrome

Skin diseases

BACKGROUND

Chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE) syndrome was first described in the scientific literature in 2010¹. A review of the literature reveals that to date this extremely rare syndrome has been reported in only 14 patients worldwide; seven males and seven females^{1,2}. Most patients developed symptoms of the disease before the age of 6 months³.

CANDLE syndrome is an autoinflammatory syndrome caused by an autosomal recessive gene mutation in PSMB8 in most identified cases, although some patients are PSMB8 mutation-negative¹. The literature indicates that there appears to be a disease spectrum of PSMB8-associated disorders including "JMP" syndrome (joint contractures, muscle atrophy, microcytic anaemia, and panniculitis-induced childhood lipodystrophy) which is also seen in

adults². Reported symptoms of CANDLE syndrome include recurrent fevers, purpuric skin lesions, periorbital erythema, violaceous eyelids, arthralgias with or without arthritis, progressive lipodystrophy, hypochromic or normocytic anaemias, hepatomegaly and failure to thrive. Other clinical features which have been described in some cases include hypertrichosis, acanthosis nigricans and alopecia areata^{3,4}. Further clinical reports of children with disease manifestations that resemble those of CANDLE syndrome have also been reported in Japan and Lebanon⁵⁻⁷.

Medical management of CANDLE syndrome includes the use of systemic steroids and NSAIDs, as well as targeted therapies including IL-1Ra, TNF α blockers, and IL-6R inhibitors; however responses to these novel therapies have been described as variable¹. Reports have indicated that although temporary clinical improvement was seen with anti-TNF and anti-IL-6 treatment, the “IFN signature” did not demonstrate improvement in most cases. The use of IL-6– blocking therapy has been shown to normalize IL-6–inducible genes and C-reactive protein levels in these patients. However, skin lesions and fatigue did not improve significantly with treatment with additional peripheral fat loss reported, suggesting a potential association between the IFN signature and disease activity⁴. It has been suggested that given the success of IL-1 blocking therapy in the treatment of other conditions, that it should be considered in the management of CANDLE syndrome. However, it has been shown that disease subsets were not responsive to IL-1 blockade⁵. Hence, deregulation of the IFN signalling pathway in patients with CANDLE syndrome has been suggested as a future target for treatment⁶. Currently, there is limited evidence available on the long term medical prognosis for patients diagnosed with CANDLE syndrome.

CLINICAL PRESENTATION

An 11 year old boy was referred to Cork University Dental Hospital for periodontal consultation, due to advanced periodontal destruction in May 2012. He had been previously diagnosed with CANDLE syndrome 2 years earlier and was undergoing treatment in Great Ormond Street Children’s Hospital, London. A significant element of the patient’s medical management included regular intravenous administration of human growth hormone (GH).

On examination, the patient was of short stature and had marked lipodystrophy of his face (Figure 1). His finger nails were malformed on both hands (Figure 2). Intra-orally, the patient had a mixed dentition with no indication of dental caries and evidence of geographic tongue. Of significance, although his oral hygiene was very good a number of his anterior teeth in both arches were severely periodontally compromised with advanced mobility (Grade III)⁸ (Figure 3). There were also significantly increased periodontal probing depths of up to 12mm around the maxillary central and lateral incisors and 10mm around the mandibular anterior teeth with evidence of severe attachment loss (Figure 4). Bleeding on probing was evident from periodontal pockets in all quadrants but there was no evidence of suppuration.

Intra-oral periapical radiographic examination confirmed significant bone loss associated with these maxillary and mandibular anterior teeth (Figure 5). Horizontal bone loss was also observed in association with the posterior teeth. A diagnosis of generalized advanced periodontitis as a manifestation of systemic disease was made.

A sibling evaluation revealed the patient’s older brother (28 years old) had also been diagnosed with CANDLE syndrome and had also received medical care in Great Ormond Street Children’s Hospital, London a number of years earlier. His medical management also included administration of systemic steroids but not GH. The patient’s brother attended for a consultation appointment and displayed a number of similar characteristics including short stature, facial lipodystrophy and malformed fingernails (Figure 6). However a clinical intra-

oral examination supported by radiographs, revealed no suggestion of active or progressive periodontal disease (Figures 7,8).

CASE MANAGEMENT

An initial treatment plan was developed for this patient including non-surgical periodontal therapy with adjunctive systemic antimicrobials. Oral hygiene instruction was provided with supragingival scaling in all quadrants. Quadrant subgingival debridement was carried out over 1 week under local anaesthetic with a 14 day course of amoxicillin (125mg/5ml oral suspension) and metronidazole (200mg/5ml oral suspension) prescribed. All pockets were irrigated with chlorhexidine gluconate after debridement. The teeth with hopeless prognosis were then extracted under local anaesthetic and immediate removable prostheses constructed (Figure 9). In total, 8 teeth were extracted: the maxillary central and lateral incisors (7, 8, 9, 10), in addition to the mandibular central and lateral incisors (23, 24, 25, 26). Post extraction healing was uneventful, and subsequently the immediate removable partial dentures were relined at chair side.

The patient is currently on periodontal maintenance therapy with a dental hygienist in the dental hospital. The emphasis of maintenance is on oral hygiene instruction, including tooth brushing technique and use of interdental bottle brushes, and denture cleansing. Non-surgical periodontal treatment is carried out every 3 months and includes disclosure of soft deposits in addition to supra-gingival and sub-gingival ultrasonic cleaning. The patient has maintained his oral hygiene moderately well with plaque scores recorded between 20-30% at each review visit. He is under review in the periodontal department on a 6 monthly basis where probing depths are recorded on a six point pocket chart. One year after initial presentation the patient's periodontal condition has remained stable with probing depths of less than 4mm recorded around his remaining teeth. In the long term, potential definitive restorative options, including dental implants, will be evaluated in discussion with the patient's medical team.

DISCUSSION

This is the first report of periodontal manifestations of CANDLE syndrome. No previous reports in the scientific literature list any oral characteristics of this rare condition. It is not clear if the periodontal manifestations were coincidental. Skin biopsies of patients with CANDLE syndrome display a characteristic neutrophilic dermatosis with a mononuclear interstitial infiltrate including "immature" neutrophils in the dermis. Histologic evaluation identifies a dense dermal infiltrate of immature neutrophils and activated macrophages. Other histological features include a dense interstitial infiltrate of mononuclear cells with nuclear atypia and both mature and immature neutrophils, with areas of karyorrhexis, as well as interstitial dermal collagen degeneration¹. These histological features have been described as pathognomonic for CANDLE syndrome^{2,3}.

The number of reported cases is small and hence it would be interesting to investigate if previously reported cases displayed a similar pattern of alveolar bone loss. In addition, future evaluation should assess if the characteristic immature neutrophil infiltrate (dermatosis) is replicated within the gingival and periodontal tissues. It could be suggested that in this patient the proteasome-associated autoinflammatory response is of significance in the periodontal tissues thus leading to advanced periodontal destruction. Further investigation could also focus on the variable expressivity of periodontal manifestations in these two siblings with confirmed CANDLE syndrome.

SUMMARY

Why is this case new information?
<ul style="list-style-type: none"> Chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE syndrome) is an extremely rare autoinflammatory syndrome Reported symptoms include: recurrent fevers, purpuric skin lesions, periorbital erythema, violaceous eyelids, arthralgias with or without arthritis, progressive lipodystrophy, hypochromic or normocytic anaemias, hepatomegaly and failure to thrive This is the first case to document any oral / periodontal manifestations of CANDLE syndrome
What are the keys to successful management of this case?
<ul style="list-style-type: none"> Management of this case necessitated a multidisciplinary approach: medical professionals, periodontist, prosthodontist and dental hygienist Periodontal treatment involved extraction of hopeless teeth, non-surgical treatment, adjunctive antimicrobials and maintenance therapy
What are the primary limitations to success in this case?
<ul style="list-style-type: none"> The challenges for this patient are maintenance of his periodontal condition and his removable prostheses Ideally, a fixed prosthodontic option would be provided for this patient but this will be considered in consultation with his supervising medical team

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Figure 1

Patient's facial profile at initial presentation with marked lipodystrophy.

Figure 2

Patient's malformed fingernails and swollen joints

Figure 3

Geographic tongue at initial presentation

Figure 4

Intraoral presentation illustrating marked recession on the upper anterior teeth (Before Picture)

Figure 5

Radiographic examination (Intra-oral periapical radiographs) of the patient's anterior teeth

Figure 6

Facial profile of patient's older brother

Figure 7

Intraoral presentation of patient's older brother. No evidence of significant gingival inflammation or inflammatory periodontal destruction noted apart from some recession.

Figure 8

Radiographic assessment of patient's older brother illustrating only mild horizontal bone loss affecting some teeth.

Figure 9

Maxillary removable prosthesis in situ after extraction of maxillary anterior teeth (After Picture)



























